PEDIATRIC PULMONARY HYPERTENSION

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1

DISCLOSURES

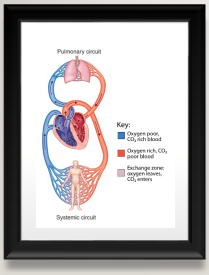
- No financial disclosures

2

OBJECTIVES

- Educate on at risk patient populations
- Share non-invasive and invasive work up
- Discuss treatment options
- Multidisciplinary approach is vital
- Share case presentation

3



ANATOMY/PHYSIOLOGY

- Right heart pumps to lungs
- Lungs perform gas exchange
- Return to left heart

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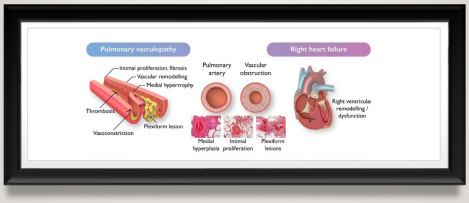

PATHOPHYSIOLOGY

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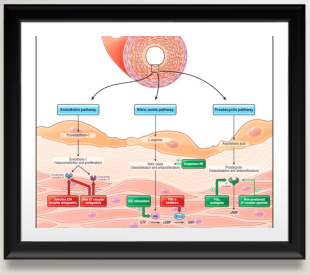


PATHOPHYSIOLOGY

- Treat 3 pathways
  - Different messenger cell stimulation and /or inhibition
- Goal is smooth muscles relaxation

6

ADVANCED PH THERAPIES

- PDE5i – Sildenafil & Tadalafil
  - Promote vasodilation
- ERA – Bosentan & Ambrisentan
  - Prevent vasoconstriction
- Prostacyclin – Epoprostenol, Treprostinil, Uptravi
  - Promote vasodilation
- *FDA approval in pediatrics limited and no approval < 1 year of age

TABLE 5 Current European Medicines Agency (EMA) and United States Food and Drug Administration (US FDA) approval status for use of pulmonary arterial hypertension drugs in paediatrics and ongoing trials

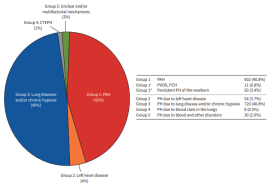
	EMA approval	FDA approval	Comments
PDE-5i			
Sildenafil	Yes	Yes	EMA: age 1–17 years FDA: age 1–17 years
Tadalafil	Yes		EMA: age >2 years
sGC stimulator			
Riociguat	Yes		EMA: >50 kg
ERA			
Bosentan	Yes	Yes	FDA: age >3 years EMA: age >1 year
Ambrisentan	Yes		EMA: age 8–18 years
Macitentan			Ongoing study
PPA			
Epoprostenol			
Treprostinil			
Selexipag (IPR-agonist)			Ongoing study
Activin signalling inhibitor			
Sotatercept			Ongoing study

PDE-5i, phosphodiesterase-5 inhibitor; sGC, soluble guanylate cyclase; ERA, endothelin receptor antagonist; PPA, prostacyclin pathway agent; IPR, selective prostacyclin receptor.

7

EPIDEMIOLOGY

- Ped PH remains rare but has high morbidity and mortality
- Incidence in US is ~6 per million children
- WHO group I – ~40% are related to CHD
- WHO group 3 – ~ 50%!!!
- Looking more – better studies, higher suspicion with genetics
  - *(BMPR2 (80%), ACVRL1, EIF2AK4, CAV1, ENG, KCNK3, SMAD9, TBX)*
- PH is a heterogenous dx with overlapping contributing factors



Group 1	PAH	692 (48.8%)
Group 1'	PVOD, PCH	11 (0.8%)
Group 1''	Persistent PH of the newborn	50 (3.4%)
Group 2	PH due to left heart disease	56 (3.7%)
Group 3	PH due to lung disease and/or chronic hypoxia	720 (48.8%)
Group 4	PH due to blood clots in the lungs	8 (0.5%)
Group 5	PH due to blood and other disorders	30 (2.0%)

AHA SCIENTIFIC STATEMENT

Pulmonary Hypertension in Congenital Heart Disease: A Scientific Statement From the American Heart Association

Pediatric Pulmonary Hypertension

Characterisation of paediatric pulmonary hypertensive vascular disease from the PPHNet Registry

8

CASE PRESENTATION

- 24-week gestation male born via C-Section due to maternal pre-eclampsia, HELLP syndrome, and poor placental growth – now 6 mo old (OSH) s/p tracheostomy and g-button
- Bronchopulmonary dysplasia, NICHD grade 3

9

WHO GROUP 3 PH – DEVELOPMENTAL LUNG DISEASE

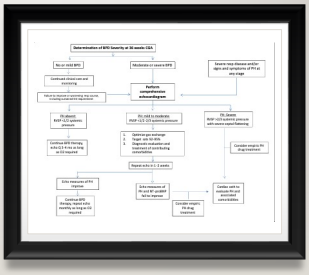
- Bronchopulmonary dysplasia (BPD) remains a major complication of prematurity.
- Pulmonary hypertension (PH) recognized as a significant problem of infants with BPD and remains strongly associated with worse outcomes and late mortality.
  - Abnormal/immature vascular structures
  - Impaired gas exchange
- Current approaches to the diagnosis and management of PH in BPD
  - Diagnosis – frequent/serial echocardiograms, CT, Cardiac cath *
  - Avoidance of chronic insults
    - Hypoxia, hypercarbia, aspiration
    - Primary treatment is aggressive treatment to support ventilation and oxygenation
    - Goal is supportive care to allow for growth over time

Pulmonary Vascular Disease and Bronchopulmonary Dysplasia: Evaluation and Treatment of Pulmonary Hypertension

10

BPD SCREENING ALGORITHM

- Screening echo at 36 weeks corrected gestational age
- Most extremely premature infant will have an echo sooner
- Repeat imaging if abnormal and consult PH team



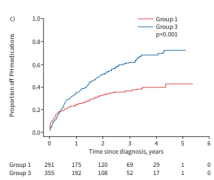
11

WHO GROUP 3

TABLE 3 Diseases associated with paediatric pulmonary hypertension (PH) with World Symposium on Pulmonary Hypertension (WSPH) Group 3 as the primary classification

Group 3: PH due to lung diseases and/or chronic hypoxia	718 (100)
3.1 Chronic obstructive pulmonary disease	4 (0.6)
3.2 Interstitial lung disease	29 (4.0)
3.2.1 Alveolar capillary dysplasia	3 (0.4)
3.2.2 Pulmonary interstitial glycogenosis	6 (0.8)
3.2.3 Surfactant protein deficiency	4 (0.6)
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern	13 (1.8)
3.4 Sleep disordered breathing	18 (2.5)
3.5 Alveolar hypoventilation disorders	3 (0.4)
3.6 Chronic exposure to high altitude	3 (0.4)
3.7 Developmental abnormalities	651 (90.4)
3.7.1 Bronchopulmonary dysplasia	320 (44.4)
3.7.2 Congenital cystic adenomatoid malformation	7 (1.0)
3.7.3 Congenital diaphragmatic hernia	256 (35.6)

Data are presented as n (%); all percentages are based on WSPH Group 3 (n=718) as the denominator. Subclasses may include overlapping or concurrent WSPH classifications.



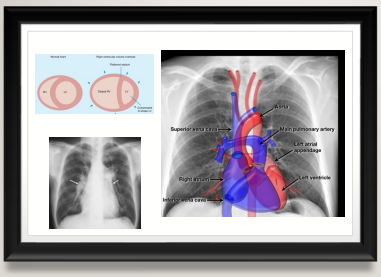
Characterisation of paediatric pulmonary hypertensive vascular disease from the PPHNet Registry

12

CASE PRESENTATION, CONT.

- 24-week gestation male, now 6 months old s/p tracheostomy with chronic respiratory failure requiring mechanical ventilation and WHO Group 3 PH
  - Arrives to our hospital and stabilizes
  - Team reviews serial echocardiograms over past 4 months and clinical course
  - Chronic CO2 retention for month with non-invasive support
  - s/p tracheostomy 1 mo ago
  - Bowel perforation was inciting event causing acute change – poor baseline
- Echocardiogram completed showing concern for RV hypertension and moderate size atrial septal defect

13



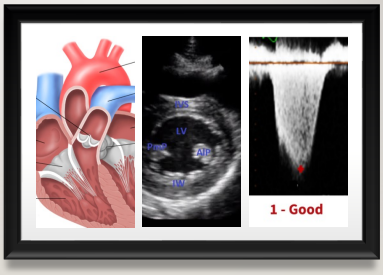
DIAGNOSTIC WORK UP

- Echocardiogram (primary tool but not definitive)
- Electrocardiogram (ECG) – RVH, tall R waves V1 V2
- CXR – r/o lung or cardiac anomalies
- 6 MWT – usually starts age 7
- Labs: CMP, CBC, proBNP, Thyroid studies

14

NORMAL ECHOCARDIOGRAM FINDINGS

- Rounded septum in systole – normal
- Tricuspid valve regurgitation (TR) – normal 2-2.5 m/second



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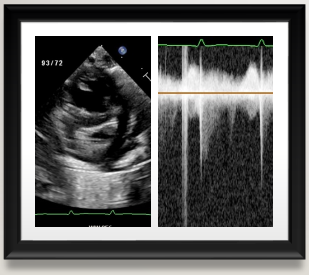


ECHO FINDINGS

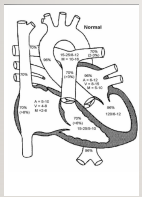
- Dilated right ventricle
- D-shaped ventricular septum
- TR 4 m/sec

16

CASE PRESENTATION, CONT.

- 24-week gestation male, now 6 months old s/p tracheostomy with chronic respiratory failure requiring mechanical ventilation and WHO Group 3 PH
- Echocardiogram completed showing concern for RV hypertension and moderate size atrial septal defect
  - Referral made to cath lab

17



CARDIAC CATHETERIZATION

- Gold standard for diagnosis of PH and is the only definitive diagnosis providing directly measured hemodynamics
  - Mean PA pressure ≥20 mmHg
  - Pulmonary capillary wedge pressure ≤ 15 mmHg
  - Pulmonary vascular resistance ≥ 3 WU x m2

Pediatric Pulmonary Hypertension

Rayya Morales-Demori, MD, FAAP; Ryan Coleman, MD; George B. Mallory, MD

Pediatr Rev (2024) 45 (5): 251–259.

https://doi.org/10.1542/pir.2023-006010

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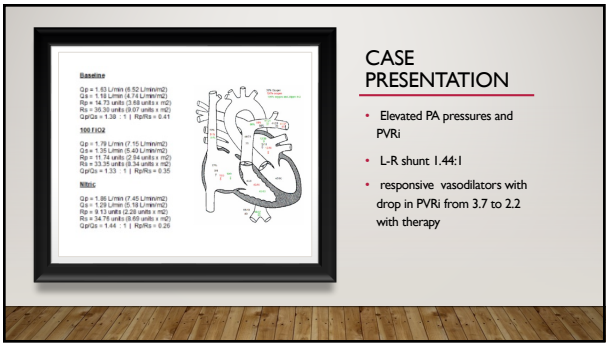

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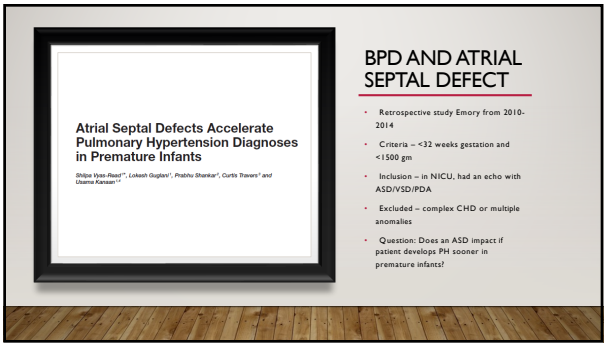

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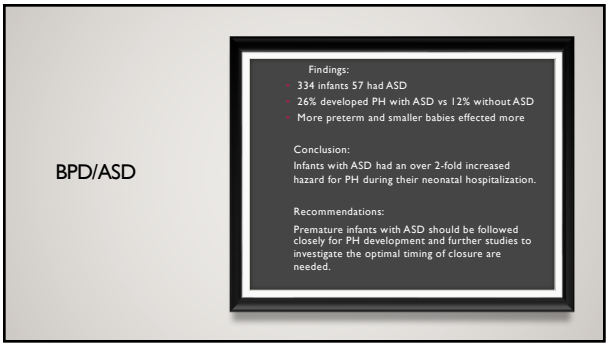

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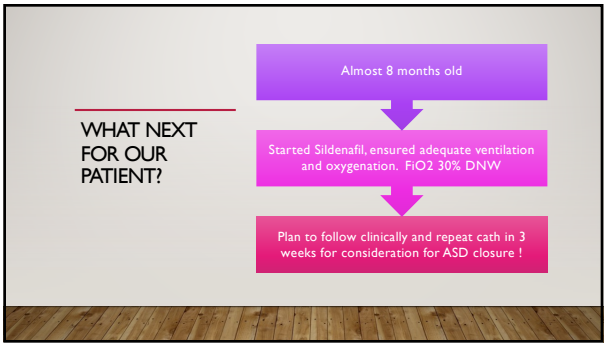

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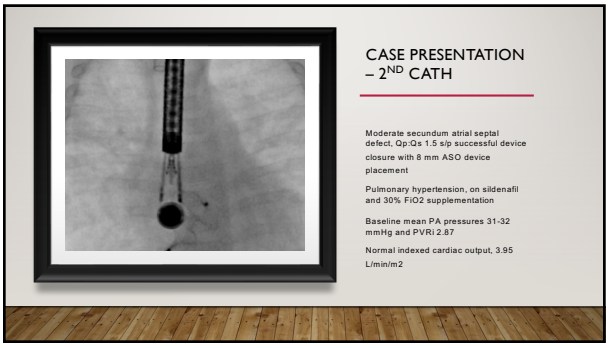

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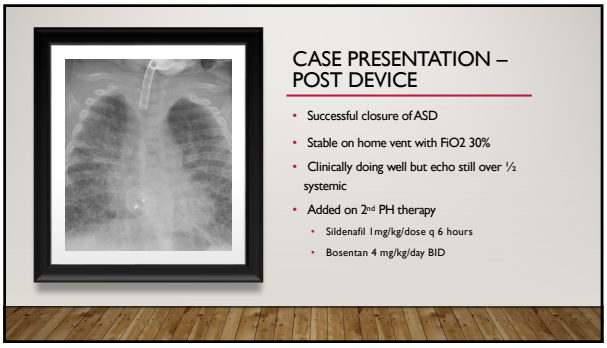
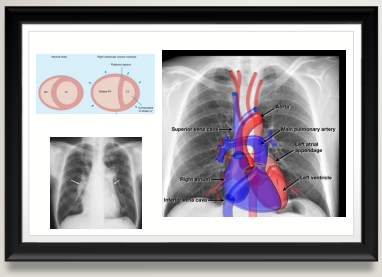


24

DISCUSSION

- Has anyone had experience with this?
- Should we consider this sooner?
- How much has this additional pulmonary blood flow impacted lung healing from a BPD standpoint?
- What do we think his trajectory will look like compared to no closure?
- How long should he stay on therapy?

25



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26

ADDITIONAL WORK UP

- Cardiac/chest CT – pulmonary veins and lung parenchymal abnormalities
- Pulmonary function tests (PFTs) – restrictive/obstructive disease
- Perfusion scan – r/o thrombus (CTEPH)
- Sleep study – evaluate for OSA — Significant contributor to PH in pediatric population

27

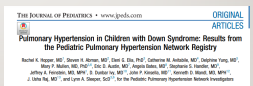
MEDICATIONS

- Entire talk itself!
- Meds aren't always the answer or the only answer
- Good RN coordinator is key
  - Work with family
  - Work with specialty pharmacy
  - Requires extensive education with family and symptom management
  - REMs programs

28

TRISOMY 21

- Most common genetic condition with ~ 5700 children born each year in the US
- 50% of patient with T21 will have a CHD
- ~ 30% of T21 patient will have PH, may be transitional (PPHN) or progressive
- Contributing factors: CHD, OSA, GERD, aspiration, recurrent URIs
- When diagnosed < 6 months of age and treated 43% had resolution
- Multidisciplinary approach is important given many contributing factors


THE JOURNAL OF PEDIATRICS • www.jpeds.com ORIGINAL ARTICLES

Pulmonary Hypertension in Children with Down Syndrome: Results from the Pediatric Pulmonary Hypertension Network Registry

29

HOW DO WE CARE FOR THESE COMPLEX KIDS

- Multi-disciplinary approach is critical
  - NICU
  - Cardiology
  - Pulmonology
  - Nephrology
  - Neurology
  - Dietitian
  - Pharmacist
  - Respiratory therapy
  - Rehab therapies
  - Palliative care

30

IMPACT ON FAMILIES

- Although rare, PH has high morbidity and mortality
- Palliative care involvement early – symptom management and progressive process
- Social work – large financial s tation

BMC Pediatrics

RESEARCH Open Access

Quantifying side effects and caregiver burdens of pediatric pulmonary hypertension therapies

Erik J. Nelson[1*], Ella Cook[1], Samara Nelton[1], Rebecca Brown[1], Morgan Pierce[1], Ashley Rangarter Sandoz[1], Heather Stickle[1] and Mitchell Johansen[1]

31

OUR TEAM

- Dr. Scott Fletcher, Dr. Trey Jantzen, Dr. Paul Sammut, Dr. Matthew Dennis, Claire Dlugosz BSN, Venus Anderson PNP-AC and the family of Hazel Nelson
- Not pictured: Jill Bechaz PharmD

32

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33